

II. AMENDMENT

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 3, 10-13, 15-23, 30-33, 37-40, 42-44, and 49 (previously canceled)

1. (previously amended) A method for producing an antibody heterodimer comprising:

(i) obtaining or constructing a DNA molecule that encodes an antibody molecule heavy chain that has binding specificity to a first antigen when said heavy chain is paired with a corresponding light chain, and introducing at least one cysteine codon into said antibody molecule heavy chain via recombinant DNA mutagenesis, wherein the location of said cysteine does not interfere with the antigen binding properties of said heterodimer;

(ii) expressing said DNA molecule in a suitable host cell, or expression system, together with a DNA molecule that encodes an antibody molecule light chain having the same specificity as the heavy chain, to produce a first antibody molecule containing said introduced cysteine residue;

(iii) purifying said first antibody molecule from said host cell or expression system;

(iv) contacting said purified first antibody molecule with an amount of a suitable reducing agent sufficient to partially reduce the intra or inter molecular disulfide bonds of said first antibody molecule to thereby enhance dimerization of said first antibody molecule with a second antibody molecule; and

(v) contacting said purified first antibody molecule with a second antibody molecule, wherein said second antibody has a binding specificity to a second antigen, wherein said second antibody contains a thiol reactive group other than a cysteine group introduced therein; and allowing sufficient time for dimerization to proceed; to thereby

2. (original) An IgG/IgG dimer produced by the method of Claim 1.
4. (original) The IgG/IgG dimer of Claim 2 which is a heterodimer.
5. (previously amended) The method of Claim 1, which results in an IgG/IgG dimer which activates components of the complement system.
6. (original) The method of Claim 1, which results in an IgG/IgG dimer that comprises the ability to activate and kill cells via the complement cascade.
7. (previously amended) The method of Claim 1, which results in an IgG/IgG dimer that binds to Fcγ receptors on cytotoxic effector cells.
8. (original) The method of Claim 7, which results in an IgG/IgG dimer that binds to Fcγ receptors on host immune cells.
9. (previously amended) The method of Claim 2 which results in an IgG/IgG dimer capable of initiating programmed cell death (apoptosis).
14. (currently amended) The dimer of Claim 2, wherein said dimer ~~is reactive against~~ comprises an antibody that binds specifically to an antigen selected from the CD23 antigen and/or the CD20 antigen
24. (previously amended) A method for producing an antibody heterodimer comprising:
 - (i) obtaining or constructing a DNA molecule that encodes an antibody molecule heavy chain that has binding specificity to a first antigen when said heavy chain is paired with a corresponding light chain, and introducing at least one cysteine codon into said antibody molecule heavy chain via recombinant DNA mutagenesis, wherein the location of said cysteine does not interfere with the antigen binding properties of said heterodimer;
 - (ii) expressing said DNA molecule in a suitable host cell, or expression system.

(iii) purifying said first antibody molecule from said host cell or expression system;

(iv) contacting said purified first antibody molecule with an amount of a suitable reducing agent sufficient to partially reduce the intra or inter molecular disulfide bonds of said first antibody molecule to thereby enhance dimerization of said first antibody molecule with a second antibody molecule; and

(v) introducing a thiol reactive group on a second antibody molecule, wherein said second antibody has a binding specificity to a second antigen, and wherein said second antibody does not have a cysteine group introduced therein; and allowing sufficient time for dimerization to proceed; to thereby produce an antibody heterodimer comprised of said first antibody molecule and said second antibody molecule, wherein each antibody molecule retains its binding specificity following dimerization.

25. (original) The method of Claim 24, wherein the thiol reactive group is a maleimido group.

26. (original) The method of Claim 24, wherein the thiol reactive group is a dithiopyridal group.

27. (original) The method of Claim 24, wherein the thiol reactive group is a reactive thiol.

28. (previously amended) An IgG/IgG dimer produced by the method of Claim 24, wherein said IgGs are of the same or different IgG subclass.

29. (original) The method of Claim 24, wherein said dimer comprises MAb molecules of different isotypes.

34. (original) The method of Claim 24, wherein said IgG/IgG dimer is a heterodimer having binding specificity for two different epitopes.

35. (currently amended) The method of Claim 34, wherein said heterodimer is ~~reactive against~~ comprises an antibody that binds specifically to the CD20 antigen, and further comprises an antibody that binds specifically to the CD23 antigen.

36. (original) The method of Claim 35, wherein said heterodimer is a C2B8/p51:8 heterodimer.

41. (previously amended) A pharmaceutical composition comprising an IgG/IgG dimer according to Claim 24, and a pharmaceutically acceptable carrier.

45. (previously amended) A method for producing an IgG/IgG heterodimer comprising preparing a first IgG MAb having binding specificity to a first antigen, introducing a cysteine residue in said first IgG MAb at a position which does not interfere with the antigen binding properties of said heterodimer, and which inhibits or prevents formation of an intramolecular disulfide bridge between sister heavy chains on the same antibody molecule, and exposing said first IgG MAb to a second IgG MAb having a binding specificity to a second antigen, whereby said first and second IgG MAbs dimerize to produce said IgG/IgG heterodimer comprised of said first IgG MAb and said second IgG MAb, wherein each IgG retains its binding specificity following dimerization.

46. (original) An IgG/IgG dimer produced by the method of Claim 45.

47. (previously added) The method of Claim 1, further comprising
(vi) terminating the reducing reaction by the addition of cysteine or other thiol blocking reagent.

48. (previously added) The method of Claim 24, further comprising
(vi) terminating the reducing reaction by the addition of cysteine or other thiol blocking reagent.

New Claims:

50. (new) A antibody heterodimer comprising at least one antibody that binds specifically to CD20 and is capable of initiating programmed cell death (apoptosis).

51. (new) The dimeric antibody of claim 50, which is an IgG/IgG dimer.

52. (new) The dimeric antibody of claim 50, comprising an antibody having a heavy chain in which at least one amino acid is replaced by cysteine at a location that does not interfere with the antigen binding properties of said dimeric antibody.

53. (new) The dimeric antibody of claim 50, wherein said at least one antibody that binds specifically to CD20 is a C2B8 antibody.

54. (new) The dimeric antibody of claim 50, further comprising an antibody that binds specifically to CD23.

55. (new) The dimeric antibody of claim 54, wherein said antibody that binds specifically to CD23 is a p5E8 antibody.

56. (new) The dimeric antibody of claim 53, further comprising an antibody that binds specifically to CD23.

57. (new) The dimeric antibody of claim 56, wherein said antibody that binds specifically to CD23 is a p5E8 antibody.

58. (new) The dimeric antibody of claim 57, which is an IgG/IgG dimer.

not interfere with the antigen binding properties of said heterodimer

60. (new) The dimeric antibody of claim 53, which is capable of initiating apoptosis of B cell lymphoma cells.

61. (new) The dimeric antibody of claim 53, which is capable of initiating apoptosis of leukemic cells of a patient with chronic lymphocytic leukemia.